Approval Date:_____

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENT TO

NEW ANIMAL DRUG APPLICATION 096-298

ADI and Tolerances for Lasalocid (AVATEC®)

In Broiler Chickens, Growing Turkeys, and Sheep

Sponsored by:

Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

NADA 096-298

FOIS-1

FREEDOM OF INFORMATION SUMMARY

ADI and Tolerances for AVATEC® in Chickens and Growing Turkeys

I. GENERAL INFORMATION:

NADA:	96-298
Sponsor:	Alpharma Inc.
Generic Names:	Lasalocid
Trade Names:	AVATEC®
Marketing Status:	OTC
Effect of Supplement:	This supplement provides for the revision 21 CFR 556.347 by establishing tolerances for residues in chicken, turkey, and sheep liver and muscle and adding an acceptable daily intake (ADI).

II. INDICATIONS FOR USE:

For the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* in broiler chickens.

For the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides* in growing turkeys.

For the prevention of coccidiosis caused by *Eimeria ovina, E. crandallis, E. ovinoidalois, (E. ninakohlyakimovae), E. parva,* and *E. intricata* in sheep.

III. DOSAGE:

A.	Dosage form:	Lasalocid is supplied as a Type A medicated article containing 90.7 grams lasalocid activity per pound.
B.	Route of Administration:	Oral, *via* the feed.
C.	Recommended Dosage:	Lasalocid is added to broiler chicken feed at concentrations from 68 to 113 g/ton for the prevention of coccidiosis caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima.*

Lasalocid is added to growing turkey feed at concentrations from 68 to 113 g/ton for the prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides.*

Lasalocid is added to sheep feed at concentrations from 20 to 30 g/ton for the prevention of coccidiosis caused by *Eimeria ovina, E. crandallis, E. ovinoidalois, (E. ninakohlyakimovae), E. parva,* and *E. intricata.*

IV. EFFECTIVENESS:

Effectiveness was established in the original approval under NADA 96-298. No additional effectiveness data were required for approval of this supplement.

V. ANIMAL SAFETY:

Target animal safety was established in the original approval under NADA 96-298. No additional target animal safety data were required for approval of this supplement.

VI. HUMAN SAFETY:

A. Toxicity Studies

The human food safety information has been updated. An Acceptable Daily Intake (ADI) of 0.01 mg/kg/day for lasalocid is established. The safe concentrations for lasalocid in chickens are revised as follows: 2.0 ppm in muscle, 6.0 ppm in liver, and 12 ppm in skin/fat. The safe concentrations for lasalocid in sheep are revised as follows: 2.0 ppm in muscle, 6.0 ppm in liver, and 12 ppm in kidney and fat. These values were determined using the procedure for setting safe concentrations for veterinary drugs published in the *Federal Register* of July 22, 1994 (Volume 59, page 27499).

B. Tolerances

The tolerance for residues of parent lasalocid in chicken skin/fat is revised from 0.3 ppm to 1.2 ppm, to reflect the updated safe concentration and additional marker reside data submitted to the Agency. Skin/fat remains the target tissue for lasalocid residues in chickens. A tolerance of 0.4 ppm for residues of parent lasalocid in chicken liver is established. These tolerances are based on data submitted under NADA 096-298 that allowed calculation of safe concentrations and are consistent with information available on residues in tissues of chickens at zero withdrawal.

A tolerance for lasalocid in turkeys was not codified for previous approvals. At this time, a tolerance of 0.4 ppm for residues of parent lasalocid in turkey liver and a tolerance of 0.4 ppm for residues of parent lasalocid in turkey skin/fat is established. These tolerances are based on data submitted under NADA 096-298 that allowed calculation of a safe concentration of 6.0 ppm in liver, 2.0 ppm in muscle, and 12 ppm in skin/fat, and are consistent with information available on residues in tissues of turkeys at zero withdrawal. The assignment of the turkey liver tolerance is based on bioavailability data described in the FOI summary for the supplement for lasalocid in turkeys (Approval Date: April 28, 1995).

Using bioavailability data from studies in the rat based on the Gallo-Torres model ("Methodology for the Determination of Bioavailability of Labeled Residues," H.E. Gallo-Torres, Journal of Toxicology and Environmental Health, 2, 827-845 (1977)), the liver total reside of human food safety concern was calculated to be 2.05 ppm. Available liver marker data were used to estimate a marker to total ratio of 6.3%, which allows a conservative calculation of the liver tolerance at 0.4 ppm.

A tolerance for lasalocid in sheep was not codified for the previous approval since the use of lasalocid in sheep qualified for a zero withdrawal. At this time, a tolerance of 1.0 ppm for residues of parent lasalocid in sheep liver is established. This tolerance is based on data submitted under NADA 096-298 that allowed calculation of a safe concentration of 6.0 ppm in liver, 2.0 ppm in muscle, and 12 ppm in fat and kidney, and is consistent with information available on tissue residue levels of parent lasalocid (marker residue) in sheep liver (target tissue) at zero withdrawal, determined in studies conducted by the sponsor before sheep were reclassified as a minor species for human food safety purposes (65 FR 47668). The assigned sheep liver tolerance reflects the 99th percentile upper tolerance limit with 95% confidence for parent lasalocid residues in the livers of sheep treated with 33 mg lasalocid/kg body weight (30 g lasalocid/ton of feed).

C. Regulatory Methods

The method available for measuring lasalocid residues down to 5 ppb in turkey liver is the regulatory HPLC method for lasalocid in chicken skin/fat and in cattle liver, which is described in the FOI summary for NADA 096-298. The method available for measuring lasalocid residues down to 25 ppb in sheep liver is the regulatory HPLC method for lasalocid in cattle liver, which is described in the FOI summary for NADA 096-298. The method is on file at the Center for Veterinary Medicine, FDA, 7500 Standish Place, Rockville, MD 20855.

VII. AGENCY CONCLUSION:

The information submitted in support of this supplement to NADA 096-298 satisfy the requirements of Section 512 of the Federal Food Drug and Cosmetic Act (FFDCA) and implementing regulations at Part 514 of Title 21 of the Code of Federal Regulations (21 CFR 514), to enable FDA to establish or update the Acceptable Daily Intake (ADI) and tolerances for parent lasalocid in chickens and growing turkeys.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food-producing animals does not qualify for exclusivity because the supplemental application does not contain new clinical or field investigations (other than bioequivalence or residue studies) and new human food safety studies (other than bioequivalence or residue studies) essential to the approval and conducted or sponsored by the applicant.

The Agency has carefully considered the potential environmental effects of this action and has concluded that the action qualifies for a categorical exclusion from the requirement to prepare an environmental assessment in accordance with 21 CFR 25.33(a)(1).